AIDS
MEMORANDUM
Acquired Immune Deficiency Syndrome

National Institute of Allergy and Infectious Diseases

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INTRODUCTION

This is the first issue of the AIDS Memorandum. This Memorandum is being published by the National Institute of Allergy and Infectious Diseases to provide a centralized forum for the rapid but informal dissemination of new clinical and experimental findings on AIDS. It is also intended that, in the Memorandum, novel ideas about the disease can be aired among members of the wide scientific audience concerned with this syndrome. To date, despite the diversity of approaches to research and treatment which have been taken by immunologists, epidemiologists, oncologists, virologists, parasitologists, internists, molecular biologists and others, AIDS remains a mysterious, devastating, lethal disease.

The AIDS Memorandum is modeled on other scientific memoranda, such as the Hepatitis, Leprosy, and Interferon Scientific Memoranda. The formats used for all memoranda include certain specific features which distinguish them from the standard journals with which every researcher is familiar. Because AIDS is a uniquely political disease, the format and the ground rules (see Page 2) devised specifically for the AIDS Memorandum consider, in addition, how proper use and accurate representation of information printed in the Memorandum can be guaranteed such that the professional interests of contributors will be protected.

The AIDS Memorandum will print preliminary data, negative findings, single case reports, and other types of material not ready or, in some cases, suitable for publication in formal journals. The expeditious sharing of these types of data may serve an important role in the eventual development of regimens for successful disease control. Material

submitted to the Memorandum will not be sent out for scientific review but will undergo review by the Memorandum's scientific and editorial staffs, so that the lag time between receipt of a manuscript and its distribution will be short (from 1 to 4 weeks). No information printed in the Memorandum can be cited except as prescribed in the ground rules. This caveat is intended to insure that publication of information in the Memorandum will in no way jeopardize or preclude future publication of refined, validated, or altered data in a formal journal. The Memorandum will be circulated only to researchers who contribute to it, so that a true information exchange can be effected.

This first issue of the Memorandum contains two articles describing experimental findings, related information about obtaining nonhuman primates for AIDS research and recommended safety precautions to be taken when experimental animals are used in AIDS studies, lists of available AIDS bibliographies and upcoming AIDS meetings, the latest case statistics reported by the Centers for Disease Control, and a questionnaire for users of the Memorandum. Future issues are expected to be more heavily weighted with original research findings. Researchers who have information to contribute can consult the Instructions for Authors found on the back page of the Memorandum.

This Memorandum is for its users. Its value and its success will depend on user participation.

GROUND RULES FOR USE OF THE AIDS MEMORANDUM

The AIDS Memorandum serves as a forum for the rapid exchange of new information and ideas among clinicians and scientists involved in AIDS research and management. Material contained in the Memorandum can be of several kinds: positive and/or negative results, clinical and/or experimental findings, preliminary and/or validated data, observations, questions, theories, commentaries, and others. This material is not subjected to peer review. Therefore, users of the Memorandum must agree to treat all material as privileged information and to consider it as tentative and subject to change prior to formal publication in a refereed journal.

Users must agree not to cite material from the Memorandum without first obtaining the consent of the author(s), and, with author permission, to cite information only as a personal communication. Author addresses are provided for this purpose.

Users must agree to contribute data or ideas to the Memorandum at least once a year. On an annual basis, the names of individuals who have not contributed to the Memorandum will be culled from the mailing list, so as to limit circulation of the Memorandum only to individuals actively working in the field.

Finally, users must agree to share material in the Memorandum only with other individuals willing to honor these ground rules.

SEARCH FOR ANTIBODY TO CANINE PARVOVIRUS (CPV) ANTIGEN IN SERA FROM AIDS PATIENTS

AIDS patients die of many different opportunistic infections. However, to date, no opportunistic organism has been shown to be the initiator of the disease syndrome. Because AIDS is a new disease,

totally unrecognized before June 1981, the possibility exists that it is caused by a new, mutant strain or recombinant agent which evolved and acquired new pathological potential and host specificity.

This report describes a study of one candidate etiologic agent, CPV. It is one of the small DNA parvoviruses, a group in which some members have shown marked evolutionary changes in both virulence and host specificity. The parvoviruses, unrecognized 15 to 18 years ago, are now found to be widespread throughout the animal kingdom.

One member of the group recently has been shown to be responsible for a number of disease syndromes in man. This virus, originally called B-19 (Cossart YE, Field AMM, Cant B, et al: Lancet, 1975, 1:72-73), has been shown to cause aplastic crises in patients with sickle cell anemia (Serjeant GR, Topley JM, Mason U, et al: Lancet, 1981, 2:595-597), hereditary spherocytosis (Kelleher JF, Luban NLC, Mortimer PP, et al: J Pediatr., 1983, 102:770-772), and pyruvate kinase deficiency (Duncan JR, Cappellini MD, Anderson MJ, et al: Lancet, 1983, 2:14-16). B-19 also has been shown to be responsible for erythema infectiosum (fifth disease) (Anderson MJ, Jones SE, Fisher-Hoch SP, et al: Lancet, 1983, 1:1378).

Another parvovirus was found to be responsible for an explosive, highly virulent, acute enteritis epidemic in dogs which occurred worldwide in 1978. The agent was new to dogs, since no antibody was found in samples collected prior to 1978. The responsible parvovirus is serologically related to feline panleukopenia virus (FPV) and to the virus which causes mink enteritis (Carmichael LE, Jourbert JC, Pollock RVH, et al: Am J Vet Res., 1980, 40:784-791). Although minor differences in these viruses allow them to be distinguished serologically, they are so closely related that they can be used reciprocally for vaccination purposes.

Another parvovirus, the minute virus of mice, has shown a marked change in both virulence and host cell preference. These changes resulted from a single mutation, a 40-50 base deletion (McMaster GK, Beard P, Engers HD, et al: J Virol., 1981, 38:317-326).

The possibility that a parvovirus could be the etiologic agent of AIDS fit with the timely appearance of CPV in the canine population and with the known ability of FPV to cross species barriers. Therefore, AIDS serum samples and various control serum samples were tested for the presence of antibody to CPV antigen.

A CPV tissue culture antigen, supplied by Dr. Leland Carmichael (State College of Veterinary Medicine, Cornell University, Ithaca, New York), was used in three in vitro assay systems: complement fixation (CF), hemagglutination inhibition (HI), and immune adherence hemagglutination (IAHA). The results of preliminary tests with dog serum samples known to be CPV positive and CPV negative are given in the table.

RECIPROCAL ANTIBODY TITER USING 4-8 ANTIGEN UNITS

Dog Serum	CF	HI	IAHA
CPV+	8	1024	1600
CPV-	<10	<10	<10

In addition to the control dog serum samples, a total of 124 human serum samples were tested. These included sera

from 42 homosexual men without AIDS, sera from 14 AIDS patients without Kaposi's sarcoma, sera from 28 AIDS patients with Kaposi's sarcoma, sera from 36 at-risk men with lymphadenopathy but not AIDS, and sera from 4 AIDS patients who used intravenous drugs. CPV antibody was not found in any of the 124 serum samples tested.

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DETERMINATION OF HELPER:SUPPRESSOR RATIOS IN CHIMPANZEE PERIPHERAL BLOOD LYMPHOCYTE SUBPOPULATIONS BY TWO-COLOR FLUORESCENT ANALYSIS

The characteristics of subpopulations of peripheral blood lymphocytes (PBLs) isolated from chimpanzees were defined and compared with the characteristics of similar cell preparations from human blood. Heparinized whole blood was layered onto gradients of Ficoll-Hypaque, and lymphocytes were collected. Surface characteristics of fresh or cryopreserved PBLs were analyzed using the fluorescence-activated cell sorter II (FACS II) and the Leu series of anti-T cell reagents: Leu 1-FITC, a pan-T cell marker; Leu 2-phycoerythrin, staining suppressor/cytotoxic cells; and Leu 3-FITC, staining helper/inducer cells. Following subpopulation enrichment, various functional assays were performed.

Chimpanzee and human PBLs were sorted, and four subpopulations were defined: I:Leu 1-, Leu 2-; II:Leu 1-, Leu 2+; III:Leu 1+, Leu 2+; IV:Leu 1+, Leu 2-. A representative sort is shown in Figure 1 for chimpanzee blood and in Figure 2 for human blood.

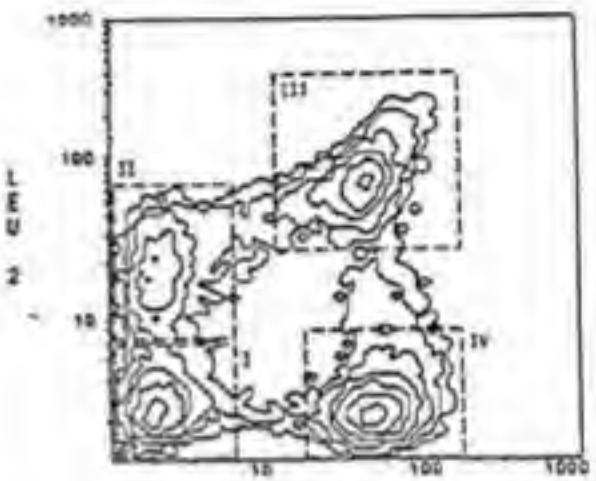


Fig. 1. Cryopreserved Unfractionated Chimpanzee Peripheral Blood

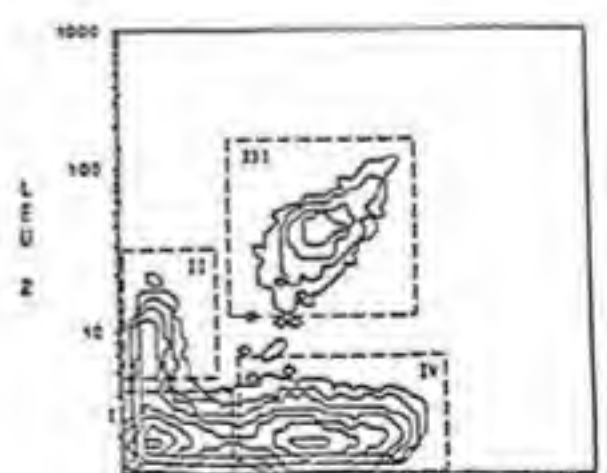


Fig. 2. Cryopreserved Unfractionated Human Peripheral Blood

A major difference in cell subpopulations was found when chimpanzee and human cells were compared. Leu 1-, Leu 2+ cells (subpopulation II) were increased in chimpanzee PBLs (Fig. 1 and Table 1) and, interestingly, were also found to be extremely high (12.5%) in human cord blood. This subpopulation accounted for only a small percentage of cells in adult human PBLs. The percentage of Leu 1-, Leu 2- cells (I) in the chimpanzee was low, and the drop compensated almost entirely for the Leu 1-, Leu 2+ cell enrichment.

TABLE 1

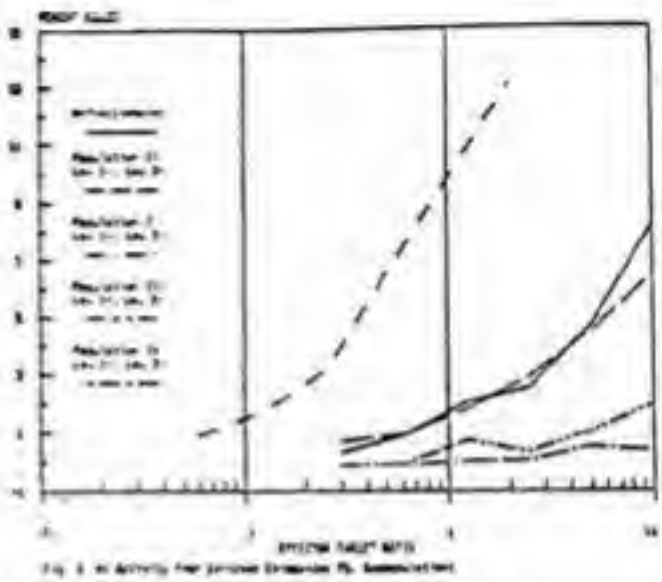
LEU 1 BY LEU 2 TWO-COLOR ANALYSIS OF PERIPHERAL BLOOD LYMPHOCYTES FROM CHIMPANZEES AND HUMANS

	Percent*		
	Adult Chimpanzee (>8 Kg)	Adolescent Chimpanzee	Adult Human
Leu 2+	31.4	24.4	22.7
Leu 1+	67.8	74.7	68.8
Leu 1+ + Leu 2+	81.7	82.9	74.6
Leu 1-, Leu 2-	18.3	17.1	25.3
Leu 1+, Leu 2-	50.3	59.5	51.9
Leu 1-, Leu 2+	13.4	8.2	5.8
Leu 1+, Leu 2+	37.5	35.2	16.9

* Average percentages from 10 humans and 8 chimpanzees.

In an experiment using all Leu 1- cells (population I plus population II) prepared from fresh cells, no proliferative activity was found when cells were incubated with three T cell mitogens, Con A, PHA, and PWM, each tested over a 100-fold range. However, all Leu 1- cells showed natural killer cell (NK) activity.

NK activity was further studied using re-sorted, enriched subpopulations. The Leu 1-, Leu 2+ subpopulation was enriched eight-fold, using a two-color quantitative sort of cryopreserved cells. NK activity was likewise enriched 8- to 10-fold (Fig. 3). Similar enrichment of Leu 1-, Leu 2- cells did not



result in comparable enrichment in NK activity. The residual NK activity found in the Leu 1-, Leu 2- population may derive from a less mature population of NK cells.

Of all the Leu 2+ cells in blood, the Leu 1-, Leu 2+ subpopulation comprised a significant fraction in adult chimpanzee samples (44%) and a smaller fraction in both adolescent chimpanzee samples (34%) and adult human samples (26%). These cells stained as suppressor/cytotoxic cells but not with a pan-T cell reagent. Their presence or absence in materials used in measuring helper:suppressor ratios markedly altered ratio values (Table 2). In addition, ratios measured

TABLE 2

HELPER-SUPPRESSOR RATIOS

	Adult Chimpanzee	Adolescent Chimpanzee	Adult Human
Leu 1+, Leu 2-: Leu 1+, Leu 2+	2.8:1	3.9:1	3.0:1
Leu 1+, Leu 2-: All Leu 2+	1.6:1	2.4:1	2.2:1

on Leu 1- cell populations which included the Leu 1-, Leu 2+ subpopulation indicated that there were differences between chimpanzee and human materials. These species differences were not seen when the Leu 1-, Leu 2+ cells were removed from the samples. This subset of cells may represent a phylogenetic (and ontogenetic?) precursor of the human NK cell.

T. Folks, D. Portnoy, L. Edison, R. Purcell, T. Chused, and K. W. Sell, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20205.

NONHUMAN PRIMATE RESOURCES FOR AIDS RESEARCH

Researchers who need help in finding nonhuman primates for AIDS studies should contact Dr. Thomas Wolfle, Executive Director, Interagency Research Animal Committee, Bldg. 12A, Room 4003, National Institutes of Health, Bethesda, MD 20205. Phone: (301) 496-5424.

The Interagency Research Animal Committee* (IRAC) can locate animals of all species of nonhuman primates. At this time, chimpanzees are the principal nonhuman primates of interest in AIDS studies: they have close evolutionary ties to humans, and they are unique among nonhuman primates in demonstrating a susceptibility to hepatitis B virus and other infectious agents. Because chimpanzees are an endangered species, only limited numbers of animals currently are available in domestic colonies.

IRAC plans to develop a registry of all nonhuman primates used in AIDS research projects. The registry will also serve as a central repository for information about ongoing AIDS studies in nonhuman primates, so that redundancy in experimental studies can be avoided.

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*IRAC, formerly IPSC, the Interagency Primate Steering Committee, was established in 1974. The committee includes representatives of the National Science Foundation, the Department of Defense, the Environmental Protection Agency, the Veterans Administration, the State Department, and the Department of Health and Human Services. The role of the committee is one of assuring that both short-term and long-term supplies of nonhuman primates will be available for biomedical research and other essential health activities.

SAFETY PRECAUTIONS FOR HANDLING EXPERIMENTAL ANIMALS USED FOR AIDS RESEARCH

The safety precautions advised for personnel involved with AIDS research were published in Morbidity and Mortality Weekly Reports in November 1982. The precautions specific to laboratory personnel handling experimental animals are reprinted here. Other portions of the recommendations will be reprinted in future issues of the AIDS Memorandum.

These precautions are advised for studies involving experimental animals inoculated with tissues or other potentially infectious materials from individuals with known or suspected AIDS.

• Laboratory coats, gowns or uniforms should be worn by personnel entering rooms in which inoculated animals are housed. Certain nonhuman primates, such as chimpanzees, may throw excreta and spit at attendants. Some animals may disturb excreta in their bedding when

they are handled. Therefore, personnel attending such animals should wear molded surgical masks and goggles or other equipment effective in preventing potentially infective droplets from reaching the mucosal surfaces of the mouth, nares and eyes.

- Personnel should wear gloves for all activities involving direct contact with experimental animals, their bedding and cages. Such manipulations should be performed carefully to minimize the creation of aerosols and droplets.
- Personnel should wear gowns and gloves for necropsy of experimental animals. If procedures are performed which generate aerosols, masks and goggles should be worn.
- Extraordinary care should be taken to avoid accidental sticks with needles or cuts with sharp instruments which may be contaminated with body fluids or tissues of experimental animals inoculated with material from AIDS patients.
- Animal cages should be decontaminated, preferably by autoclaving, before they are cleaned and washed.
- Only needle-locking syringes or one-piece needle-syringe units should be used to inject potentially infectious fluids into experimental animals.

The above precautions should be taken in both clinical and research laboratories. Biological safety cabinets and other safety equipment may not be generally available in clinical laboratories. If not, assistance should be sought from a microbiology laboratory to assure that containment is adequate to permit laboratory tests to be conducted safely.

AIDS BIBLIOGRAPHIES

Four bibliographies listing articles about AIDS are currently available.

AIDS Bibliography
(and monthly updates)
National Institute of Allergy
and Infectious Diseases
Building 5, Room 432
Bethesda, MD 20205

Free to individual scientists and clinicians and any organization.

AIDS Literature Search,
Updates and Supplements
National Library of Medicine
Reference Section
8600 Rockville Pike
Bethesda, MD 20209

Include name and address typed on a gummed label.

Gays and Acquired Immune
Deficiency Syndrome
Canadian Gay Archives
Box 639, Station A
Toronto, ON M5W 1G2
Canada

$4.00

AIDS: A Research and Clinical
Bibliography
The AIDS/KS National Foundation
54 Tenth Street
San Francisco, CA 94103

$5.00

AIDS CASES REPORTED TO THE CENTERS FOR DISEASE CONTROL AS OF AUGUST 8, 1983

UNITED STATES CASES

DISEASE	CASES	PERCENT OF TOTAL	DEATHS	PERCENT DEAD
KS without PCP	533	26.5	109	20.5
PCP without KS	1016	50.6	447	44.0
Both KS and PCP	148	7.4	80	54.1
OI without KS or PCP	311	15.5	138	44.4
TOTAL	2008	100.0	774	38.5

KS = Kaposi's sarcoma PCP = Pneumocystis carinii pneumonia
OI = Opportunistic infections

	MALES		FEMALES		TOTAL	
RISK GROUPS*	CASES	% OF TOTAL	CASES	% OF TOTAL	CASES	%
Homosexual or bisexual	1427	76.0	0	0.0	1427	71.1
IV drug user	273	14.5	66	50.8	339	16.9
Haitian	91	4.9	14	10.8	105	5.2
Hemophiliac	15	0.8	0	0.0	15	0.7
No apparent risk group or unknown	72	3.8	50	38.4	122	6.1
TOTAL	1878	100.0	130	100.0	2008	100.0

* The risk groups listed are hierarchically ordered; cases with multiple risk factors are tabulated only in the risk group listed first.

CASES REPORTED FROM OTHER COUNTRIES

NUMBER OF COUNTRIES	CASES
20	123

U.S. AND FOREIGN CASES REPORTED

TOTAL	2131

QUESTIONNAIRE FOR USERS OF THE AIDS MEMORANDUM

The questionnaire reprinted below was sent to potential users of the AIDS Memorandum. Anyone who did not receive the questionnaire at that time but would like to comment on the questions now is encouraged to send his/her comments to

AIDS Memorandum
National Institute of Allergy
and Infectious Diseases
National Institutes of Health
Building 5, Room 432
Bethesda, MD 20205

Are you familiar with the memorandum format?

If yes, have you contributed to a memorandum in the past?

Would you be willing to contribute to the AIDS Memorandum?

If no, why not?

If yes, what types of contributions would you be most likely to make?

Case reports
Positive experimental results
Negative experimental results
Positive clinical observations
Negative clinical observations
Commentaries Queries
New methodologies Theories
Others (Please describe)

Do you think this format fills a need which is not filled elsewhere?

If no, where is the need filled?
Letters to NEJM or Science
Rapid Publications in JCI
Elsewhere (Please describe)

What would make the AIDS Memorandum a valuable resource for you?

UPCOMING AIDS MEETINGS

Registration is still open for the following upcoming AIDS meetings.

NIH Workshop on the Epidemiology of AIDS
September 12-13, 1983
Holiday Inn, Crowne Plaza,
Rockville, MD

Program Information:
Robert Edelman, M.D.
(301) 496-5893
National Institute of Allergy
and Infectious Diseases
Building 31, Room 7A49
Bethesda, MD 20205
Registration Information:
Mr. Mark S. Brown
Social and Scientific Systems, Inc.
(301) 656-6346

ICAAC Symposium on AIDS
October 24-25, 1983
Las Vegas Hilton Hotel
Las Vegas, Nevada

Mr. Richard Bray
(202) 833-9680
American Society of Microbiology
1913 Eye Street, N.W.
Washington, D.C. 20006

International Conference on AIDS
November 14-17, 1983
Roosevelt Hotel, New York City

Conference Department, New York
Academy of Sciences
2 East 63rd Street
New York, NY 10021

Pre-registration by mail will begin at the end of September. Pre-registration is necessary because seating is limited.

INSTRUCTIONS FOR AUTHORS
CONTRIBUTING TO THE AIDS MEMORANDUM

Content: Articles published in the AIDS Memorandum must have obvious relevance to AIDS. They can describe clinical or experimental findings. Letters and other types of commentary are also welcome. In all cases, the text should be limited to 1000 words.

References: Refererces should be integrated into the text in parentheses. Each citation should include journal title, year of publication, volume and issue numbers and inclusive page numbers. Citations from books should include book title, editor(s), publisher, year of publication and relevant page numbers.

Tables: Whenever possible, data should be organized into tables rather than figures.

Announcements of Meetings: Announcements of upcoming AIDS meetings should include meeting title, location and date and the name, address and telephone number of the organizer of the meeting.

Further Information: For further information call the AIDS Memorandum office at (301) 496-9537.

Mailing Instructions: Manuscripts for the AIDS Memorandum should be sent to this address:

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Bethesda, Maryland 20205

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